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(54) Title: PROCESS FOR PRODUCING ENANTIOPURE  $\beta$ -AMINO ACID DERIVATIVES, AND ENANTIOPURE  $\beta$ -AMINO  
ACID DERIVATIVES

(57) Abstract: Process for producing enantiopure  $\beta$ -amino  
acid derivatives corresponding to general formula (I)  
R<sub>1</sub>-NZ-CHR<sub>2</sub>-CH<sub>2</sub>-COOR<sub>3</sub> (I) in which R<sub>1</sub> and R<sub>2</sub>  
independently denote organic residues optionally forming  
a cyclic substituent, R<sub>3</sub> denotes H or an organic residue,  
and Z represents H or an amino function-protecting group,  
comprising a step in which a mixture of enantiomers  
of a compound corresponding to general formula (II)  
R<sub>1</sub>-NZ-CHR<sub>2</sub>-CH<sub>2</sub>-COOR<sub>4</sub> (II) in which R<sub>1</sub>, R<sub>2</sub> and Z are  
as defined for formula (I), and R<sub>4</sub> is an organic residue, is  
subjected to hydrolysis in the presence of a lipase.

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GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Declarations under Rule 4.17:**

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designation US
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP2004/003688

A. CLASSIFICATION OF SUBJECT MATTER				
IPC 7	C12P41/00	C12P13/04	C12P17/14	C07K1/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, FSTA, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98/29561 A (SMITHKLINE BEECHAM PLC ;WELLS ANDREW STEPHEN (GB)) 9 July 1998 (1998-07-09) the whole document -----	1-9
X	KATAYAMA S ET AL: "Enzymatic resolution of 2-substituted tetrahydroquinolines. Convenient approaches to tricyclic quinoxalinediones as potent NMDA-glycine antagonists" TETRAHEDRON: ASYMMETRY, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 9, no. 24, 24 December 1998 (1998-12-24), pages 4295-4299, XP004150930 ISSN: 0957-4166 the whole document ----- -/-	1,2,4-9

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

### \* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

Date of the actual completion of the international search

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Date of mailing of the international search report

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Name and mailing address of the ISA

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## INTERNATIONAL SEARCH REPORT

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	FAULCONBRIDGE S J ET AL: "Preparation of enantiomerically enriched aromatic beta-amino acids via enzymatic resolution" TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 41, no. 15, April 2000 (2000-04), pages 2679-2681, XP004194578 ISSN: 0040-4039 the whole document -----	1-9
A	EP 0 605 033 A (DUPHAR INT RES) 6 July 1994 (1994-07-06) the whole document -----	1-9
A	US 5 552 318 A (HOUNG JER-YIING ET AL) 3 September 1996 (1996-09-03) the whole document -----	1-9
A	LIU M ET AL: "Recent advances in the stereoselective synthesis of beta-amino acids" TETRAHEDRON, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 58, no. 40, 30 September 2002 (2002-09-30), pages 7991-8035, XP004383841 ISSN: 0040-4020 -----	

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP2004/003688

### Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
  
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-9 (all partially and as far as applicable)

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-9 (all partially and as far as applicable)

Process for producing enantiopure beta-amino acid derivatives corresponding to general formula R1-NZ-CHR2-CH2-COOR3 in which R1 and R2 independently denote organic residues forming a cyclic substituent. Process for producing a peptide or a peptide analogue according to which the enantiopure beta-amino acid derivative is used.

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2. claims: 1-9 (all partially and as far as applicable)

Process for producing enantiopure beta-amino acid derivatives corresponding to general formula R1-NZ-CHR2-CH2-COOR3 in which R1 and R2 independently denote organic residues not forming a cyclic substituent. Process for producing a peptide or a peptide analogue according to which the enantiopure beta-amino acid derivative is used.

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3. claims: 10-12

Enantiopure beta-amino acid derivative corresponding to general formula R1-NZ-CHR2-CH2-COOR3 in which the substituents R1 and R2 form a heterocycle with the group N-Z-CH, said heterocycle comprising at least one additional hetero atom. Peptide or peptide analogue which can be obtained using, in the process for producing it, such an enantiopure beta-amino acid derivative.

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**INTERNATIONAL SEARCH REPORT**

 International Application No  
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